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Juvenile Nasopharyngeal Angiofibroma in Prepubertal Males: A Diagnostic Dilemma

P. Ryan Camilon, MD; Reza Rahbar, DMD, MD; Michael J. Cunningham, MD; Eelam A. Adil, MD, MBA

**Objectives/Hypothesis:** To highlight the presentation and management of juvenile nasopharyngeal angiofibroma (JNA) in prepubertal children.

**Study Design:** Single-institution 10-year retrospective review.

**Methods:** All identified cases of pathologically confirmed JNA in children <10 years of age were assessed from a gender, imaging and embolization findings, tumor stage, surgical approach, and clinical outcomes standpoint, and compared to a group of stage-matched older patients from the same time period.

**Results:** Of 45 patients over the 10-year study period, four male children between 8 to 9.8 years of age were identified. One patient had University of Pittsburgh Medical Center stage 1 disease, and the other three had stage 3 disease at presentation. A malignant process other than JNA was of concern preoperatively in two of the four children due to a combination of aggressive imaging characteristics and an absence of pterygopalatine fossa involvement. Such pterygopalatine fossa involvement was comparatively uniformly present in a group of stage-matched JNA patients aged 15 to 21 years. All four prepubertal children underwent surgical resection via transnasal endoscopic approach following ipsilateral sphenopalatine artery embolization without the need for blood transfusion. There were no recurrences in three of the four cases at a median follow-up duration of 2.3 years (range, 0.8–6.4 years).

**Conclusions:** JNA may pose a diagnostic challenge in prepubertal males due to the atypical age at presentation and absence of classic imaging characteristics. Successful endoscopic transnasal resection is possible despite anatomic constrictions.

**Key Words:** Juvenile nasopharyngeal angiofibroma, prepubertal, male, nasal, nasopharynx mass.

**Level of Evidence:** 4

**Laryngoscope, 129:1777–1783, 2019**

**INTRODUCTION**

Juvenile nasopharyngeal angiofibroma (JNA) is a benign fibrovascular neoplasm predominantly found in adolescent males. In the United States, the incidence of JNA accounts for 0.05% to 0.5% of all head and neck neoplasms. Histologically, JNA consists of an abundant fibrous stroma with vascular channels lined by single endothelial cells without a contractile muscular layer. Thought to arise from the sphenopalatine foramen at the junction of the pterygoid process and the sphenoid process, JNA often extends from the nasopharynx and pterygopalatine fossa into the nose, paranasal sinuses, orbit, skull base, and central nervous system. Orbital extension occurs in approximately 30% of cases by invasion through the inferior orbital fissure, and intracranial involvement occurs in 10% to 20% of cases by extension through the roof of the infratemporal fossa or through the superior orbital fissure. The classic clinical manifestations include painless nasal obstruction, recurrent unilateral epistaxis, and a nasal or nasopharyngeal mass usually present for several months prior to diagnosis. Common nonspecific symptoms include rhinorrhea, anosmia, and headache. Facial deformity, proptosis, exophthalmos, visual disturbance, cranial nerve palsies, and neurologic deficits suggest advanced disease. JNA has a predilection for adolescent and young males between the ages of 14 and 25 years. This combination of gender selectivity and age at diagnosis coinciding with puberty has historically suggested a hormonal influence. In 1959, it was first proposed that JNA development may be associated with excess androgen stimulation. Subsequent investigation focused on androgen receptors in JNA tumor cells with mixed results. No alterations in hormonal serum levels in patients with JNA have been observed, and the hormonal dependence of JNA remains controversial. Angiogenic growth factors such as vascular endothelial growth factor have more recently been associated with JNA. The potential pathophysiologic role of such nonhormonally mediated factors is viewed as a potential...
explanation for the occurrence of JNA tumors in atypical-aged patients.

Given the paucity of literature with respect to JNA in prepubescent males, we review our experience with JNA in this younger age group with respect to potentially unique clinical manifestations, imaging characteristics, and management considerations.

MATERIALS AND METHODS

A retrospective chart review of all pathology confirmed JNA cases at our institution from July 1, 2006 through July 1, 2016 was conducted. No patients were excluded. A total of 45 patients were identified during this time period. Four patients < 10 years of age were identified and further assessed from a clinical presentation, preoperative imaging, University of Pittsburgh Medical Center (UPMC) staging, surgical approach, intraoperative findings, and complications standpoint. Next, consecutive patients ≥ 10 years old with UPMC stage 1 or 3 lesions during the study period were additionally identified for comparative purposes. This study was approved by the Boston Children’s Hospital Institutional Review Board.

RESULTS

The demographic and lesion-specific characteristics of the four prepubescent patients are summarized in Table I. Three patients with UPMC stage 1 tumors and four patients with UPMC stage 3 JNAs were identified from the >10-year-old cohort for comparison to the prepubescent group (Table II).

<table>
<thead>
<tr>
<th>Age at Diagnosis (Years)</th>
<th>Laterality</th>
<th>Presenting Symptoms</th>
<th>Duration of Symptoms Prior to Presentation</th>
<th>UPMC Stage</th>
<th>Pterygopalatine Fossa Involvement?</th>
<th>Concern for Malignancy?</th>
<th>Embolized Vessel</th>
<th>EBL (mL)</th>
<th>Follow-up Time (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.8 R</td>
<td>Epistaxis, nasal obstruction</td>
<td>4 weeks</td>
<td>1</td>
<td>No</td>
<td>Yes</td>
<td>Sphenopalatine</td>
<td>850</td>
<td>6.4</td>
<td></td>
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<tr>
<td>9.8 L</td>
<td>Nasal obstruction</td>
<td>2 years</td>
<td>3</td>
<td>No</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>400</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>9.2 R</td>
<td>Nonspecific</td>
<td>1 year</td>
<td>3</td>
<td>No</td>
<td>Yes</td>
<td>Sphenopalatine</td>
<td>300</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>8.0 R</td>
<td>Epistaxis, nasal obstruction</td>
<td>7 months</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>500</td>
<td>1.4</td>
<td></td>
</tr>
</tbody>
</table>

EBL = estimated blood loss; L = left; R = right; UPMC = University of Pittsburgh Medical Center.

| Case 1 |

An 8-year-old boy presented with right nasal obstruction and ipsilateral, intermittent, significant epistaxis over 4 weeks prior to evaluation. Physical examination revealed a nasal mass at the level of the right middle meatus, extending posteriorly through the ipsilateral choana; the nasal versus nasopharyngeal origin of the lesion was difficult to identify due to its large size. Maxillofacial computed tomography (CT) and magnetic resonance imaging (MRI) were performed (Fig. 1). An intensely enhancing homogeneous mass centered within the right posterior nasal cavity and nasopharynx without involvement of the pterygopalatine fossa was identified. The signal characteristics on T2 weighted images were suggestive of a cellular or fibrous neoplasm. Although JNA was considered most likely, the child’s age and the absence of pterygopalatine fossa involvement broadened the differential diagnosis. The decision was made to proceed with embolization followed by transnasal endoscopic resection; however, his parents were counseled that a biopsy may be needed prior to resection if the angiographic features seen at the time of embolization were atypical of JNA. Angiography demonstrated a characteristic JNA pattern of vascularity with numerous fine vascular channels and an intense tumor blush. The right sphenopalatine artery (SPA) was the principal vascular supply with a very small contribution from the right ascending pharyngeal artery. The SPA was selectively embolized with Ethiodol. The patient was classified as UPMC stage 1. Transnasal endoscopic resection was performed without need for blood transfusion. MRI

| TABLE II. |

Stage-Matched Older Juvenile Nasopharyngeal Angiofibroma Cohort Case Series Summary

<table>
<thead>
<tr>
<th>Age at Diagnosis (Years)</th>
<th>Laterality</th>
<th>Presenting Symptoms</th>
<th>Duration of Symptoms Prior to Presentation</th>
<th>UPMC Stage</th>
<th>Pterygopalatine Fossa Involvement?</th>
<th>Concern for Malignancy?</th>
<th>Embolized Vessel</th>
<th>EBL (mL)</th>
<th>Follow-up Time (Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.8 R</td>
<td>Epistaxis</td>
<td>8 months</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>150</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>15.1 L</td>
<td>Nasal obstruction</td>
<td>1 year</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>350</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>17.5 R</td>
<td>Epistaxis</td>
<td>1 year</td>
<td>1</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>150</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>15.0 L</td>
<td>Epistaxis, nasal obstruction</td>
<td>1.5 years</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>400</td>
<td>4.7</td>
<td></td>
</tr>
<tr>
<td>16.1 R</td>
<td>Nasal obstruction</td>
<td>1.5 years</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>4,500</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>17.5 R</td>
<td>Epistaxis, nasal obstruction</td>
<td>6 months</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>200</td>
<td>3.8</td>
<td></td>
</tr>
<tr>
<td>21.0 R</td>
<td>Epistaxis</td>
<td>1 year</td>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>Sphenopalatine</td>
<td>450</td>
<td>3.0</td>
<td></td>
</tr>
</tbody>
</table>

EBL = estimated blood loss; L = left; R = right; UPMC = University of Pittsburgh Medical Center.
performed at 1 year and 2.5 years after surgery revealed solely postoperative changes, and he remains without recurrence on follow-up endoscopic examinations now 6.4 years postoperatively.

**Case 2**

A 9-year-old boy with intermittent left nasal obstruction for 2 years was referred to our institution for a second opinion. His outside medical records documented a...
large nasal mass presumed to be an antrochoanal polyp for which an endoscopic excision had been attempted. The procedure was aborted due to excessive hemorrhage.

Office nasal endoscopy revealed a large, friable, vascular nasal mass that originated within the left nasal airway and extended into the nasopharynx with obstruction of the contralateral choana. Both CT and MRI with contrast were obtained. These imaging studies revealed an intensely enhancing mass centered within the posterior aspect of the nasal cavity (Fig. 2A–C). The mass extended laterally into the left masticator space and eroded through the medial pterygoid plate, but spared the pterygopalatine fossa. Superiorly, it involved the sphenoid bone, specifically the region of the left vidian canal and foramen rotundum, and extended into the sphenoid sinus. The mass abutted, but did not invade, the left cavernous sinus. Inferiorly, a component of the mass extended into the oropharynx.

His endoscopic examination and imaging study findings were interpreted as consistent with JNA. Confirmatory angiography was performed with polyvinyl alcohol (PVA) particle embolization of several SPA branches of the internal maxillary artery supplying the mass. There was no residual postembolization vascularity. He was staged as UPMC stage 3 due to skull base erosion. He underwent complete transnasal endoscopic excision with 400 mL blood loss and no transfusion. Follow-up MRI and endoscopic examinations are without evidence of residual or recurrent JNA at 9 months postoperatively.

**Case 3**

A 9-year-old male with a history of allergic rhinitis presented with chronic nasal congestion and rhinorrhea. Nasal endoscopy revealed polypoid mucosal turbinate hypertrophy bilaterally. The choanae were patent bilaterally, with no significant adenoid hypertrophy and no visible masses or lesions. Medical therapy was initiated, but his symptoms persisted, prompting CT imaging. A soft tissue mass in the right posterior superior nasal cavity with osseous destruction of the right sphenoid bone and erosion of the right pterygoid body was identified (Fig. 3A,B). Given his nonspecific endoscopic findings and CT results, the concern of sarcoma, particularly rhabdomyosarcoma, prompted urgent operative biopsy. Pathology revealed fibrocollagenous stroma with numerous thin-walled vessels; specimens stained positive for CD31 and SMA, supporting the
diagnosis of JNA. Subsequent angiography was confirmatory, and right sphenopalatine artery PVA particle embolization was performed followed by transnasal endoscopic excision. He was classified as UPMC stage 3 given skull base erosion without postembolization residual vascularity. Complete resection was achieved with approximately 300 mL of blood loss without transfusion need. No residual tumor was seen on MRI performed at 3 months and 11 months after surgery. At 2.3 years postoperatively, he remains without evidence of recurrent disease based upon endoscopic assessment.

Case 4

An 8-year-old male presented with progressive right-sided nasal congestion and intermittent epistaxis over 7 months prior to evaluation. These epistaxis episodes were generally mild and self-limited. One month prior to presentation, his mother appreciated a mass within his right naris, which was confirmed on subsequent examination by an outside otolaryngologist. An MRI was obtained with findings concerning for JNA. He was referred to our institution for further evaluation and management.

Office examination revealed a completely obstructive right nasal mass preventing the passage of an endoscope through that naris. The origin of the lesion as well as the presence of mucosal invasion could not be determined. Contralateral endoscopy via the left naris revealed the mass to be extending from the right nasal passage into the nasopharynx. Review of the previously performed MRI revealed a heterogeneously enhancing mass centered within the right pterygopalatine fossa and superior aspect of the right nasal cavity consistent with a JNA (Fig. 4C). A CT scan documented the tumor to extend laterally into the right pterygomaxillary fissure, with bony destruction of the lateral wall, roof and floor of the right sphenoid sinus, right pterygoid plate, and right vidian canal (Fig. 4A,B). The SPA was confirmed on angiography to be the major vascular supply to the lesion and was successfully embolized with PVA particles. A UPMC classification stage 3 was assigned due to skull base erosion without residual vascularity. The child underwent transnasal endoscopic excision with approximately 500 mL of blood loss and no transfusion need.

A follow-up MRI performed 2 months postoperatively revealed an area of residual disease versus scar in the pterygopalatine fossa. On CT scan at 6 months, this area of concern appeared stable. MRI 11 months postoperatively documented an increase in size, consistent with residual JNA within in the right pterygopalatine fossa, now extending into the right retromaxillary fossa, infra-temporal fossa, and right pterygoid fossa. On angiography, multiple sphenoid branches off the mid internal maxillary artery and one sphenoid branch off the proximal internal maxillary artery supplied this mass. After successful embolization, transnasal endoscopic excision was performed with 50 mL of blood loss and no transfusion need.

Fig. 4. (A) Coronal and (B) axial noncontrast computed tomography images depicting an extensive lesion with bony expansion and erosion of the right pterygoid body and basisphenoid; also note the lateral extension into the pterygopalatine fossa. (C). Coronal T1 postcontrast magnetic resonance imaging confirms absence of intracranial extension.
Stage-Matched Older JNA Cohort

Three patients > 10 years old with UPMC stage 1 tumors and four patients with UPMC stage 3 JNAs were identified for comparison to the prepubescent group (Table II). The mean age of this stage-matched older patient cohort was 16.7 years. Clinical presentation and duration of symptoms were similar between the two groups, with the exception of the one prepubertal male (case 1) who presented with just 4 weeks of epistaxis. The main distinction between the groups was with regard to imaging characteristics. All of the older patients had at least medial pterygopalatine fossa involvement identified during review of their axial imaging. Based on their age of presentation and classic imaging findings, all of the older patients were diagnosed with JNA based upon clinical-coradiological criteria with no concern for malignancy.

DISCUSSION

This first case series focusing on JNA in prepubertal children highlights several potentially important observations. One is the clinical and radiologic features of JNA at presentation in this younger population may mimic those of a malignancy, particularly rhabdomyosarcoma or an alternative sarcoma. In two of the four cases (cases 1 and 3), malignancy was considered an alternative likely diagnosis. Another observation is JNA in the prepubescent population may be a more aggressive subtype than JNA in postpubertal adolescents and young adult males. The symptom duration can be quite short (e.g., 4 weeks in case 1), and the postdiagnostic course quite aggressive with rapid proliferation likewise over a short time period (e.g., 4 weeks in case 3). Of additional note, from an imaging standpoint, three of these children (cases 2, 3, and 4) had significant pterygoid bony erosion on CT assessment. Pterygoid erosion is generally thought to be a late finding of JNA progression, indicating either these lesions were present for a prolonged period, unlikely given the previous observations, or proliferated rapidly. These observations suggest JNA in prepubescent patients requires expedited evaluation and management.

PTerygopalatine fossa involvement and anterior bowing of the posterior maxillary sinus wall, known as the Holman-Miller sign, are two pathognomonic findings of JNA. Notably, both of these findings may be absent in the prepubescent JNA population. Three children in our series (cases 1, 2, and 3) did not have pterygopalatine fossa involvement on imaging. In contrast, all of the older patients had this classic imaging finding. For anterior bowing of the posterior maxillary sinus wall to develop, there must be growth of the JNA in the pterygopalatine fossa; thus, the Holman-Miller sign was absent in these three cases as well. The absence of these characteristic CT findings places a greater emphasis on contrast-enhanced MRI to elucidate the diagnosis of JNA in this patient age group. On T1-weighted images, these lesions have low signal intensity, whereas on T2-weighted images, these tumors have a heterogeneous intermediate signal intensity. Additionally, there is avid heterogeneous enhancement with flow voids when imaged with contrast.21,22

Biopsy is usually not performed prior to embolization and definitive JNA surgical resection due to the vascular nature of this lesion and the potential for resultant severe hemorrhage.23 In the vast majority of JNA cases, the diagnosis is strongly suspected based upon the age of the patient, clinical presentation, and imaging features. However, in this atypical younger age group with variable clinical presentation and absence of pathognomonic imaging findings, biopsy may be indicated. In case 1, the patient’s parents were initially counseled on the potential need to obtain a biopsy prior to resection depending upon the angiographic findings. In case 3, biopsy was performed prior to embolization due to the heightened concern of an alternate malignant diagnosis. Given the hemorrhage risk, particularly pre-embolization, biopsy should be performed in the operating suite.

The surgical approach to JNA in these younger patients may also be of concern given their smaller anatomical airway dimensions. The choice to perform an endoscopic resection versus an open approach is influenced by JNA extent and staging as well as surgeon preference. The 8- to 9-year age range of the children in this series did not preclude successful transnasal endoscopic excision.

As is true of any small number retrospective case series, the applicability of our experience to other atypical age JNA patients warrants questioning. These limitations are subject to the uncommonness of JNA itself, let alone its rarity in the prepubertal population. Our hope is this review will stimulate other institutions to report on their experiences with JNA in younger children, furthering such investigation.

CONCLUSION

JNA in prepubertal males can be a diagnostic challenge given classic patient history, and imaging findings may be absent. The duration of presenting symptoms may be shorter and the clinical progression more rapid, the latter reflected by CT documentation of submucosal pterygoid osseous erosion. With respect to imaging, pathognomonic CT findings such as pterygopalatine fossa involvement and the Holman-Miller sign may not be present, requiring a greater diagnostic reliance upon contrast-enhanced MRI. Operative biopsy may be necessary when the overall presentation raises concern of an alternative neoplastic etiology. Confirmed JNA in prepubertal children can be managed by transnasal endoscopic resection as applicable in adolescents and young adults.

BIBLIOGRAPHY


